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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,716	10/31/2003	H. William Bosch	029318-0977	8372

31049 7590 08/28/2007

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EXAMINER
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ART UNIT	PAPER NUMBER
1609	

MAIL DATE	DELIVERY MODE
08/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,716	BOSCH ET AL.	
	Examiner	Art Unit	
	Samira Jean-Louis	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-108* is/are pending in the application.

4a) Of the above claim(s) *8,15,16, 23-27 and 48-108* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-14,17-22 and 28-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Sheets (14)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 1-7, 9-14, 17-22, and 28-47 are pending in the application and are being examined on the merits herein.

Applicant's election without traverse of Group I in the reply filed on 01/29/2007 is acknowledged.

Applicant's election with traverse to various species in the reply filed on 01/29/07 is acknowledged. The traversal is on the ground(s) that the search of all the species does not impose an undue burden upon the examiner. This is not found persuasive because the claims recited in the instant application recite a multiplicity of species that are different in chemical structure and would therefore acquire separate status in the art (i.e. different classification). Thus, in this instance, these species are patentably distinct and fully capable of supporting separate patents. Furthermore, given that the claims recite such a multiplicity of species, the search would indeed be unduly extensive and burdensome given that a search for these species would consist of searching multiple databases for foreign references and literature searches.

Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 8, 15-16, 23-27, and 48-108 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group and species, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 39-40, and 42-43 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The terms "derivatives", "significantly different" and "bioequivalency" in claims 14, 39 and 42 are indefinite because the specification does not clearly redefine the term. For example, the term "derivatives" as outlined in claim 14 (i.e. polyoxyethylene castor oil derivatives) does not define which part of the parent portion remains as the compound to be used as a surface stabilizer.

In addition, the term "significantly different" does not provide a clear degree of comparison in terms of numbers, ranges or percentages.

Furthermore, the term "bioequivalency" is defined with quotation marks in claim 42 suggesting a particular meaning is to be applied; however, it is undefined in the specifications rendering it and the aforementioned terms vague and indefinite. Thus, claims 14, 39, 42 and dependent claims thereof (i.e. claims 40 and 43) are all rejected under 35 U.S.C. 112, second paragraph as vague and indefinite.

Provisional Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4-7, 9-12, 14, 18-21, and 28-47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15, 17-20, and 22-41 of copending Application No. 10683154 (hereinafter Liversidge US Patent Application No. '154). Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed to a composition comprising effective nanoparticle size of a drug characterized by desirable pharmacokinetic profiles: effective particle size after redispersibility (see claims 28-32 of instant application vs. claims 22-26 of Liversidge '154), T_{max} (see claims 33-34 of instant application vs. claims 27-28 of Liversidge '154), C_{max} (see claims 35-36 of instant application vs. claims 29-30 of Liversidge '154), higher AUC rate (see claims 37-40 of instant application vs. claims 31-34 of Liversidge '154), bioequivalent (see claims 41-43 vs. claims 35-37 of Liversidge '154) as well as viscosity (see claims 44-47

of instant application vs. claims 38-41 of Liversidge '154), all of which are due to the size of the drug.

More specifically, claims 1, 4-7, 9-12, 14, 18-21, and 28-47 of the instant application are directed to a composition comprising: sterol (triamcinalone acetonide being the elected species) with particle size less than 2000nm and a surface stabilizer.

Claims 1-15, 17-20, and 22-41 of the conflicting Liversidge '154 application are directed to a composition comprising an anti-fungal drug with particle size less than 2000nm and a surface stabilizer (other than non-ionic).

As a result, although claims 1, 4-7, 9-12, 14, 18-21, and 28-47 of the instant application are not identical to claims 1-15, 17-20, and 22-41 of the conflicting Liversidge '154 application, the aforementioned claims are not patentably distinct from each other because said claims comprise nanoparticle drugs of a size less than 2000nm characterized by increased bioavailability and redispersibility, which results in better efficacy of both drugs. Thus, one of ordinary skill would have the motivation to use "any" nanoparticulate of a drug with a stabilizer and would have a reasonable expectation that such a substitution would yield predictable results, including an enhanced pharmacokinetic profile. Thus, the aforementioned claims of the instant application are substantially overlapping in scope as discussed hereinabove and are prima facie obvious over the cited claims of corresponding application No. 10, 683, 154.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7, and 9-13 are rejected under 35 U.S.C. 102(b) as being anticipated by the work of Krause et al.

Specifically, Krause et al. teaches a composition of polylactic acid (PLA) nanoparticles of a microcrystalline salt, triamcinalone acetonide, with a mean diameter below 1 micron, a drug content from 2.9% to 8.8% w/w and a 5.5% w/w of a stabilizer (see abstract and preparation of PLA nanoparticles-pg 147). In addition, these nanoparticles of triamcinalone acetonide are further encapsulated with additional stabilizers (i.e. gelatin) and excipients (i.e. buffers) formulated as a liquid suspension. Accordingly, the teachings of Krause et al. anticipate claims 1-5, 7, 9-13.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 14, 17-22, and 28-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radhakrishnan (US Patent 5049389 and US Patent 5043165) in view Friedman (US Patent 5744155).

Radhakrishnan (US Patent 5049389) teaches a lipid particle formulation for the sustained release and delivery of steroids with improved therapeutic ratio, lower toxicity, reduced systemic side effects and stability for several months (see abstract, in particular). Specifically, Radhakrishan teaches steroids such as triamcinolone or its respective pharmaceutically acceptable salts or esters (see column 20, lines 14-15). Furthermore, Radhakrishnan teaches a composition of steroid solubilized in surfactant micelles and into small aerosol particles (see column 14, lines 47-48) that contains a non-ionic surfactant, polyoxyethylene sorbitan monolaurate (see column 14, lines 53-54) and this mixture contains steroid crystals of a size greater than 1 micron (see column 14, lines 64-65) comparable to the size recited in claims 14. Regarding biorelevant media, as recited in claims 30-32, Radhakrishnan further teaches that the

stable non-conventional liposome composition may be prepared as a suspension in a media such as water (see column 20, lines 61-65). Thus, Radhakrishnan teaches a composition of particles of triamcinolone and its pharmaceutically acceptable salts or esters of a size greater than or about 1μ containing a non-ionic surfactant as a liquid suspension in water in various concentration ranges.

While Radhakrishnan does not teach the bioadhesive property and/or characteristics of said invention; Friedman, however, discloses a water-in-oil emulsion containing submicron particles having an average particle diameter of 10-600 nm (such as a liposome) with bioadhesive properties (see abstract). Specifically this nanoparticle-containing emulsion is surrounded by a surfactant such as Tyloxapol (see Section 5.3 Composition of surfactant, column 5, lines 45-49 and instant claim 17) and further includes a bioadhesive macromolecule entailing a second surfactant such as hyrdoxypropylmethyl cellulose (referred as hypromellose in the instant claim 14) comparable to that recited in claims 18 (see Section 5.5, Bioadhesive Macromolecules, column 7, lines 10-11). This composition of Friedman further entails additional combination of steroidal and non-steroidal drugs (referred as acetylsalicylate in the instant claim) comparable to that stated in claims 20-22 (see Section 5.4, Bioactive Component, column 6, lines 6-28).

Regarding claims 28-29 and 33-47, applicant discloses in the specification that the bioavailability range, the redispersiblity range and pharmacokinetic profiles are due to the microcrystalline state of triamcinolone and its salt or ester derivatives. Thus, it can be inferred that the composition of the prior art (i.e. microcrystalline triamcinolone

acetonide) would behave similarly and entail the same characterisitics given that the prior art also discloses nanoparticles of such steroids.

Regarding claim 6, Radhakrishnan (US Patent 5043165) teaches that a composition of liposome-containing steroid can be made for topical application at the time of the claimed invention.

Though the references above do not ascribed to two separate compositions of triamcinalone acetonide as stated in claim 19, it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a third composition that is to be used for that very same purpose. Thus, the idea of combining them flows logically from their having been individually taught in prior art. Thus, claims that require no more than mixing together two compounds set forth prima facie obvious subject matter (In re Kerkhoven, 205 USPQ 1069).

Consequently, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the microcrystalline particles of triamcinolone of Radhakrisnan (US Patent 5049389), the anti-inflammatory bioactive agents and the bioadhesive polymers of Friedman and substitute it for the topical liposomal composition of Radhakrishan described in US Patent 5043165to to arrive at the composition of applicant. Given that US Patent 5043165 of Radhakrishnan teaches a steroid encapsulated liposome for topical application and Friedman teaches that additional drugs such as anti-inflammatory agents such as aspirin and additional polymers can be added to such composition, one of ordinary skill would have been motivated to

substitute the liposomes of Radhakrishnan (US Patent 5049389) and further add the additional drugs, bioadhesive polymers and excipients of Friedman to the above topical composition of Radhakrishnan with the expectation of providing a topical composition that is bioavailable, redispersible, highly absorptive, bioequivalent and possesses a high C_{max} and T_{max} comparable to that disclosed in applicant's invention.

Regarding the redispersibility, the bioequivalency, viscosity, C_{max} and T_{max} as recited in claims 28-29 and 33-47, it is considered that one of ordinary skill in the art at the time of the invention was made would have found it obvious to conclude that the microcrystalline triamcinolone acetonide composition of Krause combined with the addition of Friedman and substituted into the composition of Radhadkrishnan would possess the same pharmacokinetic profiles as that disclosed by the applicant given that these characteristics are dependent on the size of the nanoparticles of the said steroid.

It is noted that In re Best,195 USPQ 430, and In re Fitzgerald, 205 USPQ 594, discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Conclusion

Claims are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-5 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SJL

08/15/2007

Ardin H Marschel 8/17/07

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER